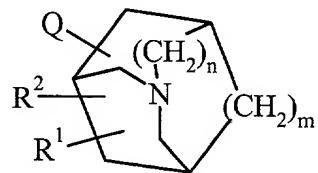


We Claim:

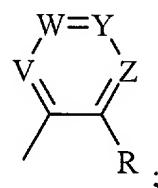
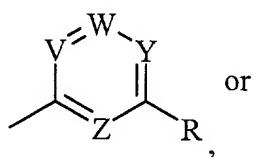
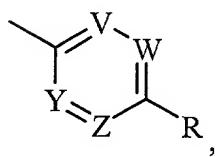
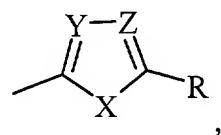
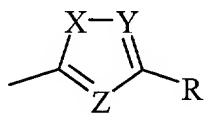
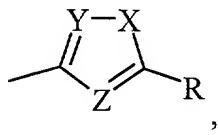
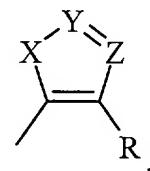
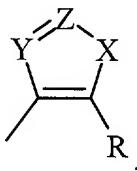
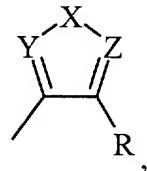
1. A pharmaceutical composition comprising at least one M4 selective muscarinic agonist selected from the azacyclic ring system having the formula I



I

including geometrical isomers, enantiomers, diastereomers, racemates, acid addition salts, salts thereof with a pharmaceutically acceptable acid, and prodrugs thereof, wherein

Q is



X is -CH₂-, -NH-, -O- or -S-;

V, W, Y and Z independently are CH or N;

n and m independently are 0, 1, 2, 3 or 4;

R¹ and R² are at any position on the azacyclic ring, including the point of attachment of the heterocycle Q, and independently are hydrogen, -OH, halogen, -NH₂, carboxy, straight or branched C₁₋₁₀-alkyl, C₁₋₁₀-alkenyl, or C₁₋₁₀-alkynyl, straight or branched C₁₋₁₀-alkoxy, or straight or branched C₁₋₁₀-alkyl substituted with -OH, -CN, -CHO, -OH, -OR³, -SR³, -

NH_2 , $-\text{NHR}^3$, $-\text{NR}^3\text{R}^4$, $-\text{NO}_2$, $-\text{SOR}^3$, $-\text{SO}_2\text{R}^3$, $-\text{COR}^3$, $-\text{CO}_2\text{R}^3$, $-\text{CONH}_2$, $-\text{CONHR}^3$, $-\text{CONR}^3\text{R}^4$, or $-\text{CH}=\text{NOR}^3$; or

R^1 and R^2 independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, $-\text{CN}$, $\text{C}_{1-10}\text{-alkyl}$, $\text{C}_{1-10}\text{-alkoxy}$, or $\text{C}_{1-10}\text{-alkylthio}$;

R is hydrogen, halogen, $-\text{CN}$, $-\text{CHO}$, $-\text{OH}$, $-\text{OR}^3$, $-\text{SR}^3$, $-\text{NH}_2$, $-\text{NHR}^3$, $-\text{NR}^3\text{R}^4$, $-\text{NO}_2$, $-\text{SOR}^3$, $-\text{SO}_2\text{R}^3$, $-\text{COR}^3$, $-\text{CO}_2\text{R}^3$, $-\text{CONH}_2$, $-\text{CONHR}^3$, $-\text{CONR}^3\text{R}^4$, or $-\text{CH}=\text{NOR}^3$; or

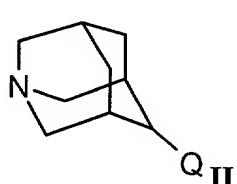
R is phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, $-\text{CN}$, $\text{C}_{1-15}\text{-alkyl}$, $\text{C}_{1-10}\text{-alkoxy}$, or $\text{C}_{1-10}\text{-alkylthio}$; or

R is a 5 or 6 membered saturated, partly saturated or aromatic heterocyclic ring containing one to three heteroatoms; and

R^3 and R^4 independently are straight, branched, or cyclic $\text{C}_{1-15}\text{-alkyl}$, $\text{C}_{2-15}\text{-alkenyl}$, $\text{C}_{2-15}\text{-alkynyl}$, or combinations thereof, or R^3 and R^4 independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl groups, each of which are unsubstituted or substituted with H, halogen, $-\text{CN}$, $\text{C}_{1-15}\text{-alkyl}$, $\text{C}_{1-10}\text{-alkoxy}$, $\text{C}_{1-10}\text{-alkylthio}$, or aryl; or

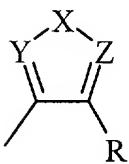
R^3 and R^4 independently are 5 or 6 membered saturated, partly saturated or aromatic heterocyclic rings containing one to three heteroatoms; and further comprising one or more additional analgesics.

2. The composition according to claim 1 wherein in formula I of the M4 selective muscarinic agonist n and m both are 1 and the azazyclic ring system has the structural formula:



wherein

Q is:



X is S,

Y and Z are N, and

R is OR³ or SR³.

3. The composition according to claim 2 wherein R³ of the M4 selective muscarinic agonist is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃ or -CH₂CH(CH₃)₂.
4. The composition according to claim 1 wherein the M4 selective muscarinic agonist is selected from the group consisting of
 - a) 3-(5-Aza-2-chlorotricyclo[3.3.1.1<3,7>]dec-2-yl)-4-chloro-1,2,5-thiadiazole;
 - b) 3-(5-Azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-chloro-1,2,5-thiadiazole;
 - c) 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-methoxy-1,2,5-thiadiazole;
 - d) 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-ethoxy-1,2,5-thiadiazole;
 - e) 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-propoxy-1,2,5-thiadiazole;
 - f) 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-butoxy-1,2,5-thiadiazole;
 - g) 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-(cyclopropylmethoxy)1,2,5-thiadiazole; and
 - h) 3-(5-azatricyclo[3.3.1.1<3,7>]dec-2-yl)-4-(2-methyl-propoxy)-1,2,5-thiadiazole;
 - i) 4-[4-(propylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane hydrochloride
 - j) 4-[4-(methylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane
 - k) 4-[4-(ethylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane

l) 4-[4-(butylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane

m) 4-[4-(2-methyl-propylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane

n) 4-[4-(cyclopropylmethylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane.

5. The composition according to claim 4 wherein the M4 selective muscarinic agonist is 4-s-[4-(propylsulfanyl)-1,2,5-thiadiazol-3-yl]-1-azatricyclo[3.3.1.1<3,7>]decane hydrochloride.

6. The composition according to claim 1 further comprising a pharmaceutically acceptable carrier.

7. The composition according to claim 1 wherein the additional analgesic is selected from the group of opioid analgesics, nonsteroidal anti-inflammatory drugs and other analgesics.

8. The composition according to claim 7 wherein the additional analgesic is an opioid analgesic.

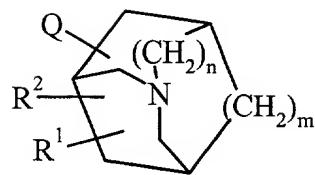
9. The composition according to claim 8 wherein the opioid analgesic is selected from the group of morphine and codeine.

10. The composition according to claim 7 wherein the additional analgesic is a non-steroidal anti-inflammatory drug.

11. The composition according to claim 10 wherein the non-steroidal anti-inflammatory drug is selected from the group of acetaminophen, ibuprofen, celoxicib and reoxicib.

12. The composition according to claim 7 wherein the additional analgesic is selected from the group of nicotinic agonists, NMDA antagonists, epileptics and alpha adrenoceptor agonists.

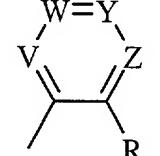
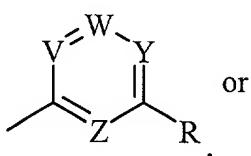
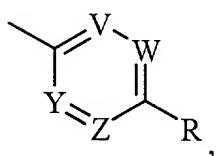
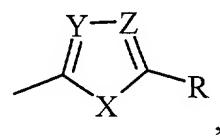
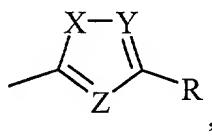
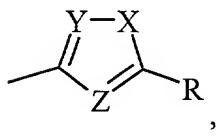
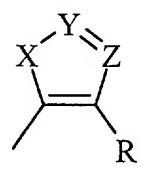
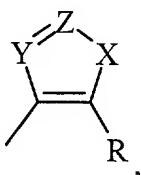
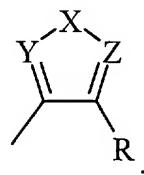
13. A method of inducing analgesia, the method comprising co-administration of at least one M4 selective muscarinic agonist selected from the azacyclic ring system having the formula I



I

including geometrical isomers, enantiomers, diastereomers, racemates, acid addition salts, salts thereof with a pharmaceutically acceptable acid, and prodrugs thereof, wherein

Q is



X is -CH₂-, -NH-, -O- or -S-;

V, W, Y and Z independently are CH or N;

n and m independently are 0, 1, 2, 3 or 4;

R¹ and R² are at any position on the azacyclic ring, including the point of attachment of the heterocycle Q, and independently are hydrogen, -OH, halogen, -NH₂, carboxy, straight or branched C₁₋₁₀-alkyl, C₁₋₁₀-alkenyl, or C₁₋₁₀-alkynyl, straight or branched C₁₋₁₀-alkoxy, or straight or branched C₁₋₁₀-alkyl substituted with -OH, -CN, -CHO, -OH, -OR³, -SR³, -NH₂, -NHR³, -NR³R⁴, -NO₂, -SOR³, -SO₂R³, -COR³, -CO₂R³, -CONH₂, -CONHR³, -CONR³R⁴, or -CH=NOR³; or

R¹ and R² independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, -CN, C₁₋₁₀-alkyl, C₁₋₁₀-alkoxy, or C₁₋₁₀-alkylthio;

R is hydrogen, halogen, -CN, -CHO, -OH, -OR³, -SR³, -NH₂, -NHR³, -NR³R⁴, -NO₂, -SOR³, -SO₂R³, -COR³, -CO₂R³, -CONH₂, -CONHR³, -CONR³R⁴, or -CH=NOR³; or

R is phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl, each of which are unsubstituted or substituted with halogen, -CN, C₁₋₁₅-alkyl, C₁₋₁₀-alkoxy, or C₁₋₁₀-alkylthio; or

R is a 5 or 6 membered saturated, partly saturated or aromatic heterocyclic ring containing one to three heteroatoms; and

R³ and R⁴ independently are straight, branched, or cyclic C₁₋₁₅-alkyl, C₂₋₁₅-alkenyl, C₂₋₁₅-alkynyl, or combinations thereof, or R³ and R⁴ independently are phenyl, phenoxy, benzoyl, benzyl or benzyloxycarbonyl groups, each of which are unsubstituted or substituted with H, halogen, -CN, C₁₋₁₅-alkyl, C₁₋₁₀-alkoxy, C₁₋₁₀-alkylthio, or aryl; or

R³ and R⁴ independently are 5 or 6 membered saturated, partly saturated or aromatic heterocyclic rings containing one to three heteroatoms; with one or more additional analgesics.

14. A method of inducing analgesia according to claim 13, the method comprising administering an analgesia-inducing amount of a composition according to claim 1 to a mammal in need thereof.
15. A composition according to claim 1 for use as a medicament.
16. A composition according to claim 1 for use as an analgesic.
17. Use of the composition according to claim 1 for the manufacture of a medicament for treatment of analgesia.